Epithalon (also known as Epitalon) is the peptide AEDG

AEDG peptides in concentrations 0.05-2.00 ng/ml on organotypic skin cell cultures proliferation in young and old animals were investigated. Peptides stimulated skin fibroblasts proliferation on 29-45% in skin cell cultures of young and old rats. https://www.ncbi.nlm.nih.gov/pubmed/25946846

[The influence of substances revealing geroprotective of spontaneous carcinogenesis in mice].

[Article in Russian]
Popovich IG.
Abstract

The review presents the results of experimental studies conducted by

the author. CBA, SHR, HER-2/neu and SAM mice revealed inhibition of age-related alterations in estrus function and spontaneous tumour development and showed **life span extension** under the influence of the pineal gland hormone Melatonin, synthetic peptide bioregulator Epitalon, delta-sleep-inducing peptide Deltaran, enterosorbent Aqualen and succinic acid containing preparation Neuronol (Noogam). The observed effect depended on the dose and conditions of administration, as well as genetic predisposition of the particular mice strains to tumour development.

https://www.ncbi.nlm.nih.gov/pubmed/15559508

Wikipedia says:

A human prospective cohort study conducted on a sample of 266 people over age 60 demonstrated that treatment with epithalamin, the pineal gland extract upon which Epitalon is based, produced a 1.6-1.8-fold reduction in mortality during the following 6 years, a 2.5-fold reduction in mortality when combined with thymulin, and a **4.1-fold reduction in mortality when combined with thymulin and administered annually** instead of only once at study onset

also:”following 3 years of biannual epithalamin treatments, as well as a **50% lower rate of cardiovascular mortality, a 50% lower rate of cardiovascular failure and serious respiratory disease,** and a 28% lower rate of overall mortality” https://en.wikipedia.org/wiki/Epitalon

I perceive that I read AEDG (epithalon) makes laboratory rodents live about 24% longer, during 2019 I found: Epithalon (0.1 microg daily 5 times a week from the age of 4 months) did not change the life span of rats living under conditions of standard day/night regimen, while in rats exposed to the natural and constant light it promoted prolongation of the maximum life span by 95 and 24 days, respectively. Epithalon prolonged the mean life span of the last 10% of rats exposed to natural and constant illumination, treated with Epithalon, by 137 and 43 days, respectively. https://www.ncbi.nlm.nih.gov/pubmed/18856211

If a rat lives about 2.5 years, then the 137 day number is about 6.6 ish % longer lifespan

Mammal studies are better, but at drosophila:
The geroprotector activity of epitalon, a synthetic tetrapeptide Ala-Glu-Asp-Gly, was studied on the Drosophila melanogaster wild strain Canton-S. The substance was added to the culture medium only at the developmental stage (from egg to larva).Epitalon significantly increased the lifespan (LS) of imagoes by 11-16% when applied at unprecedented low concentrations-from 0.001 x 10(-6) to 5 x 10(-6) wt.% of culture medium for males and from 0.01 x 10(-6) to 0.1 x 10(-6) wt.% of culture medium for females. The increase in LS did not depend on the substance dose. Effective concentrations of epitalon were 16,000-80,000,000 times lower than those of melatonin.
https://www.ncbi.nlm.nih.gov/

pubmed/11087911

The structures and metrics of peptides and the DNA double-helix cause the recognition and complementary binding of a regulatory peptide with DNA functional groups at the interface of the major groove. We have used complementary binding model to find a possible base pair sequence ATTTTC for specific binding of synthetic tetrapeptide epitalon. This base pair block and its reverse complement were found repeatedly in the promoter region of telomerase. https://www.ncbi.nlm.nih.gov/pubmed/15990728

Longevity technology:

- The peptide AEDG is published as causing greater longevity and wellness in laboratory mammals,

making a version of AEDG with weekly, monthly, annual or multi-annual dosing is beneficial.

- Fluoexetine palmitate is once weekly dosing; AEDG palmitate could be weekly dosing
- “Paliperidone Palmitate 3-month injection” suggests 3 month injection could function 3 months, noting the few nanograms or few milligrams of AEDG it is possible to think an AEDG palmitate could last longer than three months. “**Six-month depot formulation of leuprorelin acetate”** suggests 6 month AEDG dosing could be functional.
- The needleless injection technology that is like transdermal sugar dermal piercers could work at the nanograms to milligrams of AEDG to provide beneficial effect. “AEDG peptides in concentrations 0.05-2.00 ng/ml on organotypic skin cell cultures

proliferation in young and old animals were investigated. Peptides stimulated skin fibroblasts proliferation on 29-45% in skin cell cultures of young and old rats.” (PMID:25946846) suggests a therepeutic effect over a range of 1 to several hundred units of dosage having beneficial effect, that gives the possibility of the beneficial human drug being active at even transdermal needleless injection.

- The dosing amount of epithalon, AEDG might be larger than the mg dosages described at other items here. “Injectable Epithalon use (most effective): duration: 10 - 20 days dosage: between 5 - 10 mg per day”, also, “Each 10 - 20 days course of Epithalamin is followed by 4-6 months pause before repeating” (http://steroid.es/epitalon.html) suggests that 100-200 mg depot injection annually could be beneficial.

Supporting nanogram to single milligram 6 month or longer depot dosages is, “In vitro biotesting included the determination of the proliferative activity of thymocytes, a bimodal curve with the second maximum were detected at super-low doses (10(-17)-10(-15) mol/l). Authors propose a hypothesis that for superlow concentrations the formation and distance transmission of a signal from ligand to a target cell without the formation of any ligand-receptor complex take place.” (PMID:12881997)

- AEDG is orally active in rodents, it is possible AEDG toothpaste could beneficially dose humans.
- Some proteins glom to circulating albumins like SHBG strongly, it is possible that attaching AEDG to one of those proteins with a very gradually dissolving enzymatically dividable

linker could cause 1 to 3 month or greater AEDG dosing intervals and be orally administered. Oral dosing: salmon calcitonin linked peptides pass through the GI tract for oral delivery of peptides.

- I may or may not have read about injectable chemical ID, if that is non-isotopic then AEDG linked to that chemical could have annual or multiyear dosing.
- Putting an atom or a few on the AEDG peptide, like changing the =O to -OH at few places, or changing hydrophilicity or lipophilicity could make nanogram dosing possible from modifying the distance between AEDG and a cytostructure or external cytomembrane structure, rather than the activation of a receptor with AEDG, “In vitro biotesting included the determination of the proliferative activity of thymocytes, a bimodal

curve with the second maximum were detected at super-low doses (10(-17)-10(-15) mol/l). Authors propose a **hypothesis that for superlow concentrations the formation and distance transmission of a signal from ligand to a target cell without the formation of any ligand-receptor complex take place.**" (PMID:12881997)

- Variations on AEDG that do the "**to a target cell without the formation of any ligand-receptor complex"** thing at nanogram dosages: deuterated AEDG could have slightly different intramolecular distances; blood brain barrier passing version of AEDG like diacetylAEDG (possibly with enzyme degradable linker molecule),
- • Lysine-EDG (LK) is similar to AEDG, and has both similar and different effects.
- There are over 100 mentions of

epithalon, AEDG at pubmed, epithalon is a pineal peptide, there are numerous other pineal peptides that could be beneficial to humans, “Within the epiphysis polypeptide complex, free amino acids (3.26%), dipeptides (23.19%), tripeptides (50.72%), tetrapeptides (22.10%), and pentapeptides (0.72%)” The thing is though, “The biological effects of the epiphysis polypeptide complex are determined by the effect of its component AEDG”

- The peptide KED (Lys-Glu-Asp) is about 40% more effective at, “The effect of AED (Ala-Glu-Asp), KED (Lys-Glu-Asp), KE (Lys-Glu), AEDG (Ala-Glu-Asp-Gly) peptides and their compound on neuronal differentiation of human periodontal ligament stem cells (hPDLSCs) was studied by immunofluorescence and western blot analysis.” also: “Molecular aspects of

vasoprotective peptide KED activity during atherosclerosis and restenosis”

- There is also a nonapeptide, thymulin, wikipedia says, “**Thymulin**” “is a nonapeptide produced by two distinct epithelial populations in the thymus” “It requires zinc for biological activity. Its peptide sequence is H-Pyr-Ala-Lys-Ser-Gln-Gly-Gly-Ser-Asn-OH.”
- “acetylated and acetyl-amidated versions” of AEDG are described, that reminds me of acetylation to cross the blood brain barrier and possibly other cytomembranes: https://www.reddit.com/r/Nootropics/comments/3ji7d8/epitalon_any_noticeable_results/
- Also, attaching AEDG to a protein with favorable cytomembrane transport channels, likely with an enzymatically degradeable linker molecule or ATP or polyATP could cause the AEDG beneficial effects at lower doses

making annual or multiyear dosing more effective.

- nuclear membrane transport channels: Also, noting “cause the recognition and complementary binding of a regulatory peptide with DNA functional groups” **It is possible a material that causes AEDG to be preferentially transported to the nucleus through the nuclear membrane could increase the activity of AEDG at any particular dose, making annual or multiyear dosing even more effective**.
- noting, “The structures and metrics of peptides and the DNA double-helix cause the recognition and complementary binding of a regulatory peptide with DNA functional groups at the interface of the major groove. We have used complementary binding model to find a possible base pair sequence ATTTTC

for specific binding of synthetic tetrapeptide epitalon. This base pair block and its reverse complement were found repeatedly in the promoter region of telomerase.” **It is possible there are different genotypes for the ATTTTC sequence and that persons with variations can be measured as to wellness and longevity** to find an optimal version of the sequence. The more optimal sequence could then be made part of the human genome. AEDG could also be produced at human, that is persons, that is people’s tissue with gene therapy.

- Mammal and human studies could find out if **AEDG which effects melatonin production benefits the fetus and baby as much as melatonin is published as benefitting fetuses and babies**, This study notes higher fertility when

conceiving and greater resistance to trouble at the new baby, “Melatonin receptors are widespread in the embryo and fetus since early stages. There is solid evidence that **melatonin is neuroprotective and has a positive effect on the outcome of the compromised pregnancies**.” The journal article also says, “The pineal gland develops completely postpartum, so both the embryo and the fetus are dependent on the maternal melatonin provided transplacentally. Melatonin appears to be involved in the normal outcome of pregnancy beginning with the oocyte quality and finishing with the parturition” Also, “Melatonin decreases in conditions associated with serious outcome for the fetus and seems to be involved in preeclampsia and intrauterine growth restriction [**7**]. Melatonin treatment during human

normal or abnormal pregnancy has been studied for a large range of conditions and at different times during the gestational period. Considering the ethical issues, it is more difficult to study a normally occurring pregnancy, than an in vitro fertilization (IVF) one. **Melatonin administration started prior to IVF-cycles, continued during pregnancy and was associated with improved pregnancy outcomes",** also, at in vitro fertilization, "Fertilization success and pregnancy rate were improved by melatonin treatment. **Fertilization rate was 50% higher in melatonin treatment cycle**"
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4316124/

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- AEDG, epithalon is on alibaba.
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- GSK Drug delivery technology if **surgical glue is painted on a body surface does it do transdermal drug delivery** with a one time monthlong or longer lasting swab which is more advantageous than other transdermal methods. Foot area or buttock cleft or acute angle area of knee could be possible sites, with the knee angle administerable easily by the user. It might be fine on clean skin, but a thioglycollate (keratin dissolving) or microdermabrasion moist pad might be a beneficial surface prep.

  Biopolymers like prebiotic fiber transparent gels, starches, and other biopolymers are soaked in AEDG, and dried, their core remains dry and much of the peptide is shielded from aqueous environment and digestion until reaching the intestines. There

microorganisms treat the fibers or gel like prebiotics digest the fibers emitting the AEDG. Alkaline pH and having the biopolymer be purposefully positively or negatively charged like an electret could benefit both shielding and dissolving or prebiotic emission of AEDG. Also, a hydrophobic AEDG emulsion could be used to saturate the fibers, so it would be a dry lipid soaked core.

- **An AEDG as well as other peptide or protein drug transporter**: something like DMSO that transports things through the skin but is different **because it only goes 1 or 2 mm deep**; it is easy to say “diethyl or dipropyl sulfoxide” although it is possible that works. The idea is that **transporting a drug only 1 or 2 mm deep, but not further**, basically places what previously was a

transdermal applique application or effect under the skin, where it does not come off and might have characterizable dosing effect. Similarly, liposomes that only go 1 or 2 mm deep are a possible drug delivery technology: M**agnetic liposomes** exist, they could be pushed through the dermis causing a depth attaining effect only when the magnet is applied. It is also possible that lasers could drive 1-2 mm dermal transport photochemistry that causes an active drug linked to the photoactive transport molecule to diffuse at light-adjustable depth at the dermis; lipophilic to hydrophilic illumination changeable molecules could be a form; a photoactivatable zwitterion could be a form, or a drug molecule linked to a e- charge changing molecule could be a form: I perceive there are many photoactive

e- GRAS molecules, among them: chlorophyll, rhodopsin, and the version of vitamin D that uses UV to change into an active form. The active drug could be attached to the light driven molecule with an endogenously available body enzyme degradeable linker molecule, ATP, or polyATP that separates the active drug from the photomigrating molecule.

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- It is possible that as AEDG is only four amino acids long that yeast or yogurt bacteria could be **bred purposefully to produce it**; I perceive yeast and bacteria secrete peptides, to their media as well as harbored endogenously at the microorganism, to make AEDG at a microorganism with breeding: the existing highest amount of mg per volume produced peptide that is secreted that the organism produces, at possibly 4-7

amino acids long could be the high volume secretion or endogenous cytoplasm peptide to modify to produce AEDG; exposing a microrganism to a mutagen like UV then screening a bunch of microarray culture plates to find those that had replaced the first of their already produced, high volume secreted peptides' amino acids to be alanine (The A in AEDG), then reculturing those at a new array of microarray culture plates, exposing to a mutagen until the next amino acid produced was an E, then continue cycling until D and G were produced in the sequence AEDG is a way to do this. **I also favor directly genetically engineering AEDG of an orally available form like salmon calcitonin linked AEDG to be in a common deliciousness enhanced plant or even a weed species.**

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- Previously described is a transparent michael reaction (henna effect) chemical reaction with keratin at dermis (notably at beauty peptides and sunsceen) which causes much longer lasting dosing, this could be used with the nanogram doses of AEDG, if nanogram dosing is quantitatively measured as heightening wellness and producing greater longevity.
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  Chewels and white chocolate as AEDG snacks, noting that .5 to 250 units of AEDG activity is published as beneficial, if you eat 10 candy treats or 5000 candy treats you are ok. Also once every few months (human AEDG dosing every 6 months at one study) you get to eat more candy, and knowing it is beneficial to you, many food concerns might be ignored. You

could even click on “get a subscription and twice a year you get chewels and white chocolate as you prefer” online. Chewels are yummy fluid centered gum; they squirt in your mouth when you chew on them. They could be filled with an AEDG shielding emulsion at hydrolyzed or dry fiber or variously a biopolymer (beta glucans or starch, artificial microtapioca); The spurty gelid delicious chewels flavor experience contains 5 mg of AEDG each, so two chewels three times a day.

At one published study on AEDG (where the human dose is described) it describes 10mg three times a day for ten or twenty days, and then 6 months between sessions. That is 300 to 600 mg per AEDG treatment unit. At 1 mg per white chocolate treat you get to eat three groups of

ten white chocolate treats a day, the thing is if you eat 40 treats a day you are still at the effective beneficial dose range (.5 to 250 units) for AEDG and get to eat lots of treats.

There is published literature on orally available peptides. It is possible the technologies that make a particular variation on vasopressin causes 75 times more absorption at double strength could be utilized at AEDG, “Modifications of individual amino acids combined with the substitution of one more L-amino acid with D-amino acids can significantly alter physiological properties. This was demonstrated by vasopressin analogs 1-deamino-8-D-arginine vasopressin (DDAVP) and [Val4, D-Arg8], arginine-vasopressin (dVDAVP), hereafter called desmopressin and deaminovasopressin, respectively.

While the former involves deamination of the first amino acid and replacement of the last L-arginine with D-arginine, the latter also has the fourth amino acid changed to valine. While the natural vasopressin is orally active in the water-loaded rat at large doses, desmopressin is twice as active at the 75th fraction of the dose, which is attributed to enhanced membrane permeation and enzymatic stability. Desmopressin absorption was shown to be passive and by the paracellular route across the rat jejunum and site dependent in rabbits. Whether the chemical modification alters the transport pathway, however, remains to be unknown”
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2792531/

A plurality of technologies I have thought of utilize enzymatically

dividable linker molecules, sometimes between an active drug and a transporter molecule. At some areas like cytoplasm applications like making multiparallel molecule transport versions of a drug I perceive value; Some other applications like peptide and protein drugs, among them AEDG, may benefit from highly affordable, mass consumable, thrifty to manufacture drug emitting systems. AEDG Soaked fibers or an emulsion that separates at a higher pH part of the intestines could be more value effective to manufacture as compared with a sequentially reacted peptide-enzymatically dividable linker-salmon calcitonin molecule.

At peptide transport, shielding from stomach acid, an edible biopolymer like beta glucans, starch, or

hydrolyzed fiber could be advantageous. pre-colon intestines are higher pH and have bacteria that treats some kinds of fiber as prebiotic nutrients. These bacteria soften and ingest the fiber releasing the AEDG from the dry or lipid emulsion soaked core area at the intestines.

Along with the quantifiable AEDG emission of dry core fibers is the emulsion technology. edible oil or other gooey lipid is pressed into the fiber, reaching the dry core, which is now a hydrophobic oily drug transporting core. with AEDG absorbed onto biopolymers or prebiotic fibers or even hydrolyzed fiber , with or without an emulsion, which emits 1 to 3 mg of dose for each 3 mg of AEDG and absorbed at the gi tract after it gets prebiotically digested and emulsified at the

intestines, separating the lipid from the biopolymer (like beta glucans or starch or fiber gel) that the AEDG is adsorbed on causes the AEDG to desorb from the biopolymer surface. Also, it is my perception that biopolymers can be positively or negatively charged, causing the AEDG to cling to them rather than diffuse and agitate out from peristalsis.

It seems kind of direct, but AEDG soaked biopolymer, perhaps actual fiber similar to the transparent fiber in existing human fiber supplements, such that the core of the fiber is dry or lipid emulsion aqueous contact reduced has emittable AEDG unexposed to stomach contents, could release the AEDG when bacteria digest the fiber, prebiotic style.

The fibers could be made at various

diameters if AEDG is quantitatively measured as being its most effective, longevizing, and wellness producing at a steady plasma curve: a few sizes of diameters of fibers would make some prebioticized and emitted rapidly while others would emit AEDG hours later.

AEDG Soaked fibers or an emulsion that separates at a higher pH part of the intestines could be value effective to manufacture as compared with a sequentially reacted peptide-enzymatically dividable linker-salmon calcitonin molecule. I have read that attaching a peptide to salmon calcitonin produces effective oral delivery of peptide drugs. There is also an oral form of vasopressin available.

AEDG dosing at about 9.2-18.4 cents

annually: A thing of generic multivitamins is near $7, a 2019 AD guide to people’s value point. So **what is the actual manufacturing $ to produce an AEDG tetrapeptide dose sequence**: It is possible it is about 4 to 8 cents. Online collagen peptides are $43 for 20 oz., very similar to a number of drug peptides, are $8.95 per 100 grams, so 8.95 cents a gram, and each twice annual dose is 300 to 600 mg, so about 2.6 to 5.3 cents for the actual AEDG at the product, or less than 11 cents a year. Note, even if four times the AEDG is used to produce a unit dose, from absorption, reaction with intestineal contents, and other amount of drug that reaches the circulatory system effects that is near 21 cents a year for the active ingredient. Making the varied diameter fibers that are prebioticized,

and are soaked with pH and time release AEDG it is plausible that filter paper is a value model; At some amount of quality, that is near $1 for 100 grams. So that is 1 cent a gram, and if each dose of AEDG occupies a fortieth of the mass of the prebioticized fiber then 300-600 mg becomes 12 to 24 grams of fiber for each semiannual dose or 2 to 4 cents for the prebioticized fiber per AEDG dose sequence.
At manufacture then, a full AEDG dose sequence is 4.6 to 9.2 cents to manufacture. Twice annually that is 9.2 to 18.4 cents year. Noting that generic multivitamins are near $7, the earnings is 38-76 times higher than how much $ to produce the product.

Also, published material says, oral“**desmopressin is twice as active at the 75th fraction of the**

dose”
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2792531/, so it is my perception that oral drug delivery of AEDG and thymulin is possible; the published 150 times more effective oral dose efficiency compared with the unmodified peptide, combined with the .5 to 250 dose units to produce benefit at AEDG, causes a potency range where 1.6 (250/150) to .0033 (.5/150) is the range of published AEDG dosage amounts at the 150 times efficacy of the oral vasopressin peptide.

Another peptide, the nonapeptide thymulin could be combined with AEDG to quadruple the reduction in mortality.

Benefit: AEDG caused “a 2.5-fold reduction in mortality when combined

with thymulin, and a **4.1-fold reduction in mortality when combined with thymulin and administered annually** instead of only once at study onset”
https://en.wikipedia.org/wiki/Thymulin